

-29-

CLAIMS

What is claimed is:

1. A compound of formula (I),

5 $(R^2 R^3) - A^7 - A^8 - A^9 - A^{10} - A^{11} - A^{12} - A^{13} - A^{14} - A^{15} - A^{16} - A^{17} - A^{18} - A^{19} - A^{20} - A^{21} - A^{22} - A^{23} - A^{24} - A^{25} - A^{26} - A^{27} - A^{28} - A^{29} - A^{30} - A^{31} - A^{32} - A^{33} - A^{34} - A^{35} - A^{36} - A^{37} - R^1$,

(I)

wherein

A⁷ is L-His, Ura, Paa, Pta, D-His, Tyr, 3-Pal, 4-Pal, Hppa, Tma-His, Amp or deleted,
 provided that when A⁷ is Ura, Paa, Pta or Hppa then R² and R³ are deleted;

A⁸ is Ala, D-Ala, Aib, Acc, N-Me-Ala, N-Me-D-Ala, Arg or N-Me-Gly;

A⁹ is Glu, N-Me-Glu, N-Me-Asp or Asp;

A¹⁰ is Gly, Acc, Ala, D-Ala, Phe or Aib;

A¹¹ is Thr or Ser;

A¹² is Phe, Acc, Aic, Aib, 3-Pal, 4-Pal, β-Nal, Cha, Trp or X¹-Phe;

A¹³ is Thr or Ser;

A¹⁴ is Ser, Thr, Ala or Aib;

A¹⁵ is Asp, Ala, D-Asp or Glu;

A¹⁶ is Val, D-Val, Acc, Aib, Leu, Ile, Tle, Nle, Abu, Ala, D-Ala, Tba or Cha;

A¹⁷ is Ser, Ala, D-Ala, Aib, Acc or Thr;

A¹⁸ is Ser, Ala, D-Ala, Aib, Acc or Thr;

A¹⁹ is Tyr, D-Tyr, Cha, Phe, 3-Pal, 4-Pal, Acc, β-Nal, Amp or X¹-Phe;

A²⁰ is Leu, Ala, Acc, Aib, Nle, Ile, Cha, Tle, Val, Phe or X¹-Phe;

A²¹ is Glu, Ala or Asp;

A²² is Gly, Acc, Ala, D-Ala, β-Ala or Aib;

A²³ is Gln, Asp, Ala, D-Ala, Aib, Acc, Asn or Glu;

A²⁴ is Ala, Aib, Val, Abu, Tle or Acc;

A²⁵ is Ala, Aib, Val, Abu, Tle, Acc, Lys, Arg, hArg, Orn, HN-CH((CH₂)_n-NR¹⁰R¹¹)-C(O) or HN-CH((CH₂)_e-X³)-C(O);

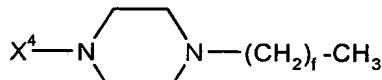
A²⁶ is Lys, Ala, 3-Pal, 4-Pal, Arg, hArg, Orn, Amp, HN-CH((CH₂)_n-NR¹⁰R¹¹)-C(O) or HN-CH((CH₂)_e-X³)-C(O);

A²⁷ is Glu, Ala, D-Ala or Asp;

A²⁸ is Phe, Ala, Pal, β-Nal, X¹-Phe, Aic, Acc, Aib, Cha or Trp;

-30-

- A²⁹ is Ile, Acc, Aib, Leu, Nle, Cha, Tle, Val, Abu, Ala, Tba or Phe;
A³⁰ is Ala, Aib, Acc or deleted;
A³¹ is Trp, Ala, β-Nal, 3-Pal, 4-Pal, Phe, Acc, Aib, Cha, Amp or deleted;
A³² is Leu, Ala, Acc, Aib, Nle, Ile, Cha, Tle, Phe, X¹-Phe, Ala or deleted;
- 5 A³³ is Val, Acc, Aib, Leu, Ile, Tle, Nle, Cha, Ala, Phe, Abu, X¹-Phe, Tba, Gaba or deleted;
A³⁴ is Lys, Arg, hArg, Orn, Amp, Gaba, HN-CH((CH₂)_n-NR¹⁰R¹¹)-C(O), HN-CH((CH₂)_e-X³)-C(O) or deleted;
A³⁵ is Gly or deleted;
- 10 A³⁶ is L- or D-Arg, D- or L-Lys, D- or L-hArg, D- or L-Orn, Amp, HN-CH((CH₂)_n-NR¹⁰R¹¹)-C(O), HN-CH((CH₂)_e-X³)-C(O) or deleted;
A³⁷ is Gly or deleted;
- 15 X¹ for each occurrence is independently selected from the group consisting of (C₁-C₆)alkyl, OH and halo;
- R¹ is OH, NH₂, (C₁-C₁₂)alkoxy, or NH-X²-CH₂-Z⁰, wherein X² is a (C₁-C₁₂)hydrocarbon moiety, and Z⁰ is H, OH, CO₂H or CONH₂;



X³ is or -C(O)-NHR¹², wherein X⁴ for each occurrence is independently -C(O)-, -NH-C(O)- or -CH₂-; and f for each occurrence is independently an integer from 1 to 29;

- 20 each of R² and R³ is independently selected from the group consisting of H, (C₁-C₃₀)alkyl, (C₂-C₃₀)alkenyl, phenyl(C₁-C₃₀)alkyl, naphthyl(C₁-C₃₀)alkyl, hydroxy(C₁-C₃₀)alkyl, hydroxy(C₂-C₃₀)alkenyl, hydroxyphenyl(C₁-C₃₀)alkyl, and hydroxynaphthyl(C₁-C₃₀)alkyl; or one of R² and R³ is C(O)X⁵ in which X⁵ is (C₁-C₃₀)alkyl, (C₂-C₃₀)alkenyl, phenyl(C₁-C₃₀)alkyl, naphthyl(C₁-C₃₀)alkyl, hydroxy(C₁-C₃₀)alkyl, hydroxy(C₂-C₃₀)alkenyl, hydroxyphenyl(C₁-C₃₀)alkyl,
- 25 hydroxynaphthyl(C₁-C₃₀)alkyl, (CH₃)₂-N-C=N(CH₃)₂.

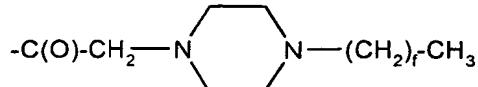


(a)

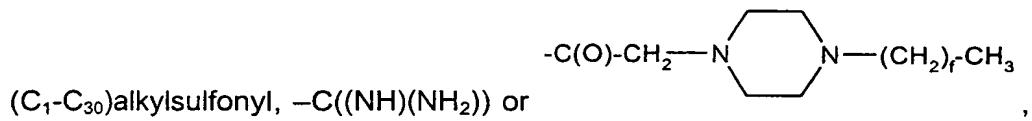
(b)

-31-

where Y is H or OH, r is 0 to 4 and q is 0 to 4;
e for each occurrence is independently an integer from 1 to 4;
n for each occurrence is independently an integer from 1-5; and
R¹⁰ and R¹¹ for each occurrence is each independently H, (C₁-C₃₀)alkyl, (C₁-C₃₀)acyl, (C₁-C₃₀)alkylsulfonyl, -C((NH)(NH₂)) or



, provided that when R¹⁰ is (C₁-C₃₀)acyl,



R¹¹ is H or (C₁-C₃₀)alkyl; and

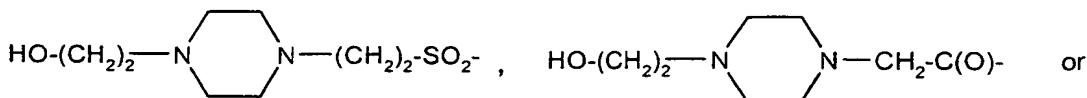
R¹² is (C₁-C₃₀)alkyl;

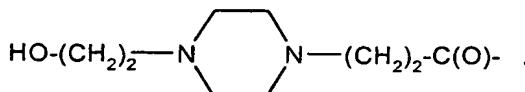
10 with the proviso that:

- (i) at least one amino acid of a compound of formula (I) is not the same as the native sequence of hGLP-1(7-36, or -37)NH₂ (SEQ ID NOS: 1, 2) or hGLP-1(7-36, or -37)OH (SEQ ID NOS: 3, 4);
- (ii) a compound of formula (I) is not an analogue of hGLP-1(7-36, or -37)NH₂ (SEQ ID NOS: 1,2) or hGLP-1(7-36, or -37)OH (SEQ ID NOS: 3, 4) wherein a single position has been substituted by Ala;
- (iii) a compound of formula (I) is not [Lys²⁶(N^c-alkanoyl)]hGLP-1(7-36, or -37)-E (SEQ ID NOS: 5-8), [Lys³⁴(N^c-alkanoyl)]hGLP-1(7-36, or -37)-E (SEQ ID NOS: 9-12), [Lys^{26,34}-bis(N^c-alkanoyl)]hGLP-1(7-36, or -37)-E (SEQ ID NOS: 13-16), [Arg²⁶, Lys³⁴(N^c-alkanoyl)]hGLP-1(8-36, or -37)-E (SEQ ID NOS: 17-20), or [Arg^{26,34}, Lys³⁶(N^c-alkanoyl)]hGLP-1(7-36, or -37)-E, wherein E is -OH or -NH₂ (SEQ ID NOS: 21-24);
- (iv) a compound of formula (I) is not Z¹-hGLP-1(7-36, or -37)-OH, Z¹-hGLP-1(7-36, or -37)-NH₂, where Z¹ is selected from the group consisting of
 - (a) [Arg²⁶] (SEQ ID NOS: 25-28), [Arg³⁴] (SEQ ID NOS: 29-32), [Arg^{26,34}] (SEQ ID NOS: 33-36), [Lys³⁶] (SEQ ID NOS: 37-40), [Arg²⁶, Lys³⁶] (SEQ ID NOS: 41-44), [Arg³⁴, Lys³⁶] (SEQ ID NOS: 45-46), [D-Lys³⁶], [Arg³⁶] (SEQ ID NOS: 37-40), [D-Arg³⁶], [Arg^{26,34}, Lys³⁶] (SEQ ID NOS: 49-52), or [Arg^{26,36}, Lys³⁴] (SEQ ID NOS: 25-28);
 - (b) [Asp²¹] (SEQ ID NOS: 53-56);

-32-

- (c) at least one of [Aib⁸] (SEQ ID NOS: 57-60), [D-Ala⁸] and [Asp⁹] (SEQ ID NOS: 61-64); and
 - (d) [Tyr⁷] (SEQ ID NOS: 65-68), [N-acyl-His⁷] (SEQ ID NOS: 69-72), [N-alkyl-His⁷] (SEQ ID NOS: 73-76), [N-acyl-D-His⁷] or [N-alkyl-D-His⁷];
 - 5 (v) a compound of formula (I) is not a combination of any two of the substitutions listed in groups (a) to (d); and
 - (vi) a compound of formula (I) is not [N-Me-Ala⁸]hGLP-1(8-36 or -37) (SEQ ID NOS: 77, 78), [Glu¹⁵]hGLP-1(7-36 or -37) (SEQ ID NOS: 79, 80), [Asp²¹]hGLP-1(7-36 or -37) (SEQ ID NOS: 53, 54) or [Phe³¹]hGLP-1(7-36 or -37) (SEQ ID NOS: 81, 82).
- 10 2. A compound according to claim 1 or a pharmaceutically acceptable salt thereof wherein A¹¹ is Thr; A¹³ is Thr; A¹⁴ is Ser, Aib or Ala; A¹⁷ is Ser, Ala, Aib or D-Ala; A¹⁸ is Ser, Ala, Aib or D-Ala; A²¹ is Glu or Ala; A²³ is Gln, Glu, or Ala; and A²⁷ is Glu or Ala.
- 15 3. A compound according to claim 2 or a pharmaceutically acceptable salt thereof wherein A⁹ is Glu, N-Me-Glu or N-Me-Asp; A¹² is Phe, Acc or Aic; A¹⁶ is Val, D-Val, Acc, Aib, Ala, Tle or D-Ala; A¹⁹ is Tyr, 3-Pal, 4-Pal or D-Tyr; A²⁰ is Leu, Acc, Cha, Ala or Tle; A²⁴ is Ala, Aib or Acc; A²⁵ is Ala, Aib, Acc, Lys, Arg, hArg, Orn, HN-CH((CH₂)_n-NH-R¹⁰)-C(O); A²⁸ is Phe or Ala; A²⁹ is Ile, Acc or Tle; A³⁰ is Ala, Aib or deleted; A³¹ is Trp, Ala, 3-Pal, 4-Pal or deleted; A³² is Leu, Acc, Cha, Ala or deleted; A³³ is Val, Acc, Ala, Gaba, Tle or deleted.
- 20 4. A compound according to claim 3 or a pharmaceutically acceptable salt thereof wherein A⁸ is Ala, D-Ala, Aib, A6c, A5c, N-Me-Ala, N-Me-D-Ala or N-Me-Gly; A¹⁰ is Gly, Ala, D-Ala or Phe; A¹² is Phe, A6c or A5c; A¹⁶ is Val, Ala, Tle, A6c, A5c or D-Val; A²⁰ is Leu, A6c, A5c, Cha, Ala or Tle; A²² is Gly, Aib, β-Ala, L-Ala or D-Ala; A²⁴ is Ala or Aib; A²⁹ is Ile, A6c, A5c or Tle; A³² is Leu, A6c, A5c, Cha, Ala or deleted; A³³ is Val, A6c, A5c, Ala, Gaba, Tle or deleted.
- 25 5. A compound according to claim 4 or a pharmaceutically acceptable salt thereof wherein R¹ is OH or NH₂.
6. A compound according to claim 5 or a pharmaceutically acceptable salt thereof wherein R² is H and R³ is (C₁-C₃₀)alkyl, (C₂-C₃₀)alkenyl, (C₁-C₃₀)acyl,





7. A compound according to claim 1 wherein said compound is
 [D-Ala⁸, Ala^{17,22,23,27}, 3-Pal^{19,31}, Gaba³⁴]hGLP-1(7-34)-NH₂;
 [D-Ala^{8,23,27}, 3-Pal^{19,31}]hGLP-1(7-35)-NH₂;
- 5 [Ala^{18,23,27}, 3-Pal^{19,31}]hGLP-1(7-35)-NH₂ (SEQ ID NO: 83);
 [Ala^{16,23,27}, 3-Pal^{19,31}]hGLP-1(7-35)-NH₂ (SEQ ID NO: 84);
 [Ala^{14,23,27}, 3-Pal^{19,31}]hGLP-1(7-35)-NH₂ (SEQ ID NO: 85);
 [Ala^{22,23,27}, 3-Pal^{19,31}]hGLP-1(7-35)-NH₂ (SEQ ID NO: 86);
 [Hppa⁷]hGLP-1(7-36)-NH₂ (SEQ ID NO: 87);
- 10 [Ala^{15,23,27}, 3-Pal^{19,31}]hGLP-1(7-35)-NH₂ (SEQ ID NO: 88);
 [Ala^{17,23,27}, 3-Pal^{19,31}]hGLP-1(7-35)-NH₂ (SEQ ID NO: 89);
 [Ala^{22,23,27}, 3-Pal^{19,31}, Gaba³⁴]hGLP-1(7-34)-NH₂ (SEQ ID NO: 90);
 [Ala^{15,22,23,27}, 3-Pal^{19,31}, Gaba³⁴]hGLP-1(7-34)-NH₂ (SEQ ID NO: 91);
 [Ala^{17,22,23,27}, 3-Pal^{19,31}, Gaba³⁴]hGLP-1(7-34)-NH₂ (SEQ ID NO: 92);
- 15 [Ala^{18,22,23,27}, 3-Pal^{19,31}, Gaba³⁴]hGLP-1(7-34)-NH₂ (SEQ ID NO: 93);
 [Ala^{21,22,23,27}, 3-Pal^{19,31}, Gaba³⁴]hGLP-1(7-34)-NH₂ (SEQ ID NO: 94);
 [Ala^{22,23,26,27}, 3-Pal^{19,31}, Gaba³⁴]hGLP-1(7-34)-NH₂ (SEQ ID NO: 95);
 [Ala^{22,23,27,32}, 3-Pal^{19,31}, Gaba³⁴]hGLP-1(7-34)-NH₂ (SEQ ID NO: 96);
 [Ala^{22,23,26,27}, 3-Pal^{19,31}, Gaba³³]hGLP-1(7-33)-NH₂ (SEQ ID NO: 97);
- 20 [Ala^{22,23,27,31}, 3-Pal¹⁹, Gaba³³]hGLP-1(7-33)-NH₂ (SEQ ID NO: 98);
 [Ala^{22,23,27,28}, 3-Pal^{19,31}, Gaba³³]hGLP-1(7-33)-NH₂ (SEQ ID NO: 99);
 [Ala^{22,23,27,29}, 3-Pal^{19,31}, Gaba³³]hGLP-1(7-33)-NH₂ (SEQ ID NO: 100);
 [Ala^{23,27}, 3-Pal^{19,31}, Gaba³³]hGLP-1(7-33)-NH₂ (SEQ ID NO: 101);
 [Ala^{20,22,23,27}, 3-Pal^{19,31}, Gaba³³]hGLP-1(7-33)-NH₂ (SEQ ID NO: 102);
- 25 [Ala^{22,23,27}, 3-Pal^{19,31}, Gaba³³]hGLP-1(7-33)-NH₂ (SEQ ID NO: 103);
 [Ala^{17,22,23,27}, 3-Pal^{19,31}, Gaba³³]hGLP-1(7-33)-NH₂ (SEQ ID NO: 104);
 [D-Ala¹⁰, Ala^{22,23,27}, 3-Pal^{19,31}, Gaba³³]hGLP-1(7-33)-NH₂;
 [D-Ala⁸, Ala^{17,23,27}, 3-Pal^{19,31}]hGLP-1(7-34)-NH₂;
 [Ala^{17,23,27}, 3-Pal^{19,26,31}]hGLP-1(7-34)-NH₂ (SEQ ID NO: 105);
- 30 [D-Ala⁸, Ala¹⁷, 3-Pal^{19,31}]hGLP-1(7-34)-NH₂;
 [Ala^{17,23,27}, 3-Pal^{19,31}]hGLP-1(7-34)-NH₂ (SEQ ID NO: 106);
 [D-Ala⁸, Ala^{17,23,27}, 3-Pal^{19,31}, Tle²⁹]hGLP-1(7-34)-NH₂;

-34-

- [D-Ala⁸, Ala^{17,23,27}, 3-Pal^{19,31}, Tle¹⁶]hGLP-1(7-34)-NH₂;
- [D-Ala⁸, Ala^{17,23,27}, 3-Pal^{19,31}, Gaba³⁴]hGLP-1(7-34)-NH₂;
- [D-Ala²², Ala^{17,23,27}, 3-Pal^{19,31}, Gaba³⁴]hGLP-1(7-34)-NH₂;
- [Aib⁸, Ala^{17,23,27}, 3-Pal^{19,31}, Gaba³⁴]hGLP-1(7-34)-NH₂ (SEQ ID NO: 107);
- 5 [D-Ala⁸, Ala^{17,22,23,27}, 3-Pal^{19,31}]hGLP-1(7-33)-NH₂;
- [Aib⁸, Ala^{17,22,23,27}, 3-Pal^{19,31}]hGLP-1(7-33)-NH₂ (SEQ ID NO: 108);
- [Ala^{17,18,23,27}, 3-Pal^{19,31}, Gaba³⁴]hGLP-1(7-34)-NH₂ (SEQ ID NO: 109);
- [Ala^{17,23,27}, 3-Pal^{19,31}, Tle³³, Gaba³⁴]hGLP-1(7-34)-NH₂ (SEQ ID NO: 110);
- [Tle¹⁶, Ala^{17,23,27}, 3-Pal^{19,31}, Gaba³⁴]hGLP-1(7-34)-NH₂ (SEQ ID NO: 111);
- 10 [N-Me-D-Ala⁸, Ala^{17,22,23,27}, 3-Pal^{19,31}]hGLP-1(7-33)-NH₂;
- [Aib⁸, Ala^{17,18,22,23,27}, 3-Pal^{19,31}]hGLP-1(7-33)-NH₂ (SEQ ID NO: 112);
- [Ala^{17,18,22,23,27}, 3-Pal^{19,31}, Tle^{16,20}, Gaba³⁴]hGLP-1(7-34)-NH₂ (SEQ ID NO: 113);
- [D-Ala⁸, Ala^{17,18,22,23,27}, 3-Pal^{19,31}, Tle¹⁶, Gaba³⁴]hGLP-1(7-34)-NH₂;
- [D-Ala^{8,22}, Ala^{17,18,23,27}, 3-Pal^{19,31}, Gaba³⁴]hGLP-1(7-34)-NH₂;
- 15 [D-Ala^{8,18}, Ala^{17,22,23,27}, 3-Pal^{19,31}, Gaba³⁴]hGLP-1(7-34)-NH₂;
- [D-Ala^{8,17}, Ala^{18,22,23,27}, 3-Pal^{19,31}, Gaba³⁴]hGLP-1(7-34)-NH₂; or
- [D-Ala⁸, Ala^{17,18,22,23,27}, 3-Pal^{19,31}, Gaba³⁴]hGLP-1(7-34)-NH₂; or a pharmaceutically acceptable salt thereof.
8. A compound according to claim 1 wherein said compound is
- 20 [Aib⁸, A6c³²]hGLP-1(7-36)NH₂ (SEQ ID NO: 114);
- [A6c^{20,32}]hGLP-1(7-36)-NH₂ (SEQ ID NO: 115);
- [Aib⁸]hGLP-1(7-36)-NH₂ (SEQ ID NO: 116);
- [(Tma-His)⁷]hGLP-1(7-36)-NH₂ (SEQ ID NO: 117);
- [A6c⁸]hGLP-1(8-36)-NH₂ (SEQ ID NO: 118);
- 25 [A6c⁸]hGLP-1(7-36)-NH₂ (SEQ ID NO: 119);
- [A6c^{16,20}]hGLP-1(7-36)-NH₂ (SEQ ID NO: 120);
- [A6c^{29,32}]hGLP-1(7-36)-NH₂ (SEQ ID NO: 121);
- [A6c²⁰, Aib²⁴]hGLP-1(7-36)-NH₂ (SEQ ID NO: 122);
- [Aib²⁴, A6c^{29,32}]hGLP-1(7-36)-NH₂ (SEQ ID NO: 123);
- 30 [A6c^{16,29,32}]hGLP-1(7-36)-NH₂ (SEQ ID NO: 124);
- [Ura⁷]hGLP-1(7-36)-NH₂ (SEQ ID NO: 125);
- [Paa⁷]hGLP-1(7-36)-NH₂ (SEQ ID NO: 126);
- [Pta⁷]hGLP-1(7-36)-NH₂ (SEQ ID NO: 127);
- [N-Me-Ala⁸]hGLP-1(7-36)-NH₂ (SEQ ID NO: 128);

-35-

- [N-Me-Ala⁸]hGLP-1(8-36)-NH₂ (SEQ ID NO:);
[N-Me-D-Ala⁸]hGLP-1(7-36)-NH₂;
[N-Me-D-Ala⁸]hGLP-1(8-36)-NH₂;
[N-Me-Gly⁸]hGLP-1(7-36)-NH₂ (SEQ ID NO: 129);
5 [A5c⁸]hGLP-1(7-36)-NH₂ (SEQ ID NO: 130);
[N-Me-Glu⁹]hGLP-1(7-36)-NH₂ (SEQ ID NO: 131);
[A5c⁸, A6c^{20,32}]hGLP-1(7-36)-NH₂ (SEQ ID NO: 132);
[Aib⁸, A6c³²]hGLP-1(7-36)-NH₂ (SEQ ID NO: 133);
[Aib^{8,25}]hGLP-1(7-36)-NH₂ (SEQ ID NO: 134);
10 [Aib^{8,24}]hGLP-1(7-36)-NH₂ (SEQ ID NO: 135);
[Aib^{8,30}]hGLP-1(7-36)-NH₂ (SEQ ID NO: 136);
[Aib⁸, Cha²⁰]hGLP-1(7-36)-NH₂ (SEQ ID NO: 137);
[Aib⁸, Cha³²]hGLP-1(7-36)-NH₂ (SEQ ID NO: 138);
[Aib⁸, Glu²³]hGLP-1(7-36)-NH₂ (SEQ ID NO: 139);
15 [Aib⁸, A6c²⁰]hGLP-1(7-36)-NH₂ (SEQ ID NO: 140);
[Aib⁸, A6c^{20,32}]hGLP-1(7-36)-NH₂ (SEQ ID NO: 141);
[Aib^{8,22}]hGLP-1(7-36)-NH₂ (SEQ ID NO: 142);
[Aib⁸, β-Ala²²]hGLP-1(7-36)-NH₂ (SEQ ID NO: 143);
[Aib⁸, Lys²⁵]hGLP-1(7-36)-NH₂ (SEQ ID NO: 144);
20 [Aib⁸, A6c¹²]hGLP-1(7-36)-NH₂ (SEQ ID NO: 145);
[Aib⁸, A6c²⁹]hGLP-1(7-36)-NH₂ (SEQ ID NO: 146);
[Aib⁸, A6c³³]hGLP-1(7-36)-NH₂ (SEQ ID NO: 147);
[Aib^{8,14}]hGLP-1(7-36)NH₂ (SEQ ID NO: 148);
[Aib^{8,18}]hGLP-1(7-36)NH₂ (SEQ ID NO: 149);
25 [Aib^{8,17}]hGLP-1(7-36)NH₂ (SEQ ID NO: 150); or
[Aib⁸, D-Arg;²⁶]hGLP-1(7-36)NH₂; or a pharmaceutically acceptable salt thereof.

9. A pharmaceutical composition comprising an effective amount of a compound according to claim 1 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier or diluent.

30 10. A method of eliciting an agonist effect from a GLP-1 receptor in a subject in need thereof which comprises administering to said subject an effective amount of a compound according to claim 1 or a pharmaceutically acceptable salt thereof.

-36-

11. A method of treating a disease selected from the group consisting of Type I diabetes, Type II diabetes, obesity, glucagonomas, secretory disorders of the airway, metabolic disorder, arthritis, osteoporosis, central nervous system disease, restenosis, neurodegenerative disease, renal failure, congestive heart
5 failure, nephrotic syndrome, cirrhosis, pulmonary edema, and hypertension, in a subject in need thereof which comprises administering to said subject an effective amount of a compound according to claim 1 or a pharmaceutically acceptable salt thereof.

12. A method according to claim 11 wherein said disease is Type I
10 diabetes or Type II diabetes.

15